1648

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

GUICHARD et al. Atty. Ref.: 1487-25; Confirmation No. 7913

Appl. No. 09/549,186 TC/A.U. 1648

Filed: April 13, 2000 Examiner: Parkin

For: RETRO PEPTIDES, ANTIBODIES THERETO AND THEIR USES FOR VACCINATION AND IN VITRO DIAGNOSIS

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March 14, 2005

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

SUPPLEMENTAL SUBMISSION

Supplemental to the Amendment filed February 16, 2005, attached is a Declaration of Lawrence K. Silbart and the noted Curriculum Vitae in support of the Amendment.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____
B. J. Sadoff
Reg. No. 36,663

BJS:
1100 North Glebe Road, 8th Floor
Arlington, VA 22201-4714
Telephone: (703) 816-4000
Facsimile: (703) 816-4100

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For: RETRO PEPTIDES, ANTIBODIES THERETO AND THEIR USES FOR VACCINATION AND IN VITRO DIAGNOSIS

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

DECLARATION

I, Lawrence K. Silbart, do hereby declare and say as follows:

1. I am an Adjunct Associate Professor of Veterinary Medicine at Tufts University School of Veterinary Medicine, North Grafton, Massachusetts. A copy of my Curriculum Vitae is attached. MY PRIMARY ACADEMIC APPOINTMENT IS AT THE UNIVERSITY OF CONNECTICUT, STORRS, CT 06269-4163

2. I have reviewed the above-identified application.

3. It is my understanding that the above-identified application describes a vaccine containing an immunoretroid form of an immunologically active peptide, the

immunoretroid being a derivative of the immunologically active peptide which binds to an antibody or an antibody fragment to the peptide with at least an equal affinity as the peptide; wherein the immunoretroid form is a retro-inverso peptide or a retro-peptide of a peptide, wherein the immunoretroid form of the peptide has the following formula II:

$$A\text{-}CH(R_i)\text{-}NH\text{-}[CO\text{-}CH(R_k)\text{-}NH]_{j-i}\text{-}CO\text{-}CH(R_{j+1})\text{-}B \quad (II)$$

wherein

n, which is the number of aminoacyl residues in formula II, is 20, and R_i , R_k, and R_{j+1} are side chains of the aminoacyl residues,

i, j and k are whole numbers

wherein $1 \leq i \leq j < n$, and

if i=j, k=0; and

if $i < j$, $i + 1 \leq k \leq j$;

such that,

where $i = 1$ and $j + 1 = n$, A is Q and B is M;

where $i = 1$ and $j + 1 \neq n$, A is Q and B is L;

where $i \neq 1$ and $j + 1 = n$, A is T and B is M; and

where $i \neq 1$ and $j + 1 \neq n$, A is T and B is L;

Q being selected from the group H-, H_2N-, P-HN-, RR'N-, H_2NCO-, RR'NCO-, RCO-;

M being selected from the group H-, -COOH, -COOR, -$CONH_2$, -CONRR' and -NHCOR;

L being -CO-NH-CH(R_{j+2})-CO-...-NH-CH(R_n)-CO-Y

wherein Y is selected from the group -OH, -OR, -NH_2, and -NRR'; and

T being X-HN-CH(R_1)-CO-...-NH-CH(R_{l-1})CO-NH-

wherein X is selected from the group H-, P-, R- and RCO-;

wherein

R and R' are independently selected from the group of hydrogen, C_{1-25} alkyl, C_{3-25} allyl, C_{6-25} aryl, benzyl, 2-phenyl-ethyl, methyl-fluorenyl, glycolamide and benzhydrylglycolamide; and

P is a protecting group; and

wherein the immunoretroid form is a retro-inverso peptide or a retro-peptide of a peptide selected from the following group:

FP peptide of serotype A12 of foot-and-mouth disease virus,

FL peptide of serotype A12 of foot-and-mouth disease virus, and

SL peptide of serotype A12 of foot-and-mouth disease virus,

wherein the vaccine further contains a physiologically acceptable vehicle.

4. It is my understanding that the above-identified application describes a composition containing an immunoretroid form of a peptide selected from the following group: FP peptide of serotype A12 of foot-and-mouth disease virus, FL peptide of serotype A12 of foot-and-mouth disease virus, and SL peptide of serotype A12 of foot-and-mouth disease virus, the immunoretroid being a derivative of the peptide which binds to an antibody or an antibody fragment to said peptide with at least an equal affinity as the peptide; wherein the immunoretroid form is a retro-inverso peptide or a retro-peptide of a peptide, wherein said immunoretroid form of the peptide has the following formula II:

$$A\text{-}CH(R_i)\text{-}NH\text{-}[CO\text{-}CH(R_k)\text{-}NH]_{i-j}\text{-}CO\text{-}CH(R_{j+1})\text{-}B \quad (II)$$

wherein

n is 20,

i is a whole number in the range of 1-19,

j is a whole number in the range of 1-19,

k is 0 or whole number in the range of 2-19,

and R_i, R_k, and R_{j+1} are side chains of the aminoacyl residues of the peptide,

wherein $1 \leq i \leq j < n$, and

If i=j, k=0; and

If $i < j$, $i + 1 \leq k \leq j$;

such that,

where $i = 1$ and $j + 1 = n$, A is Q and B is M;

where $i = 1$ and $j + 1 \neq n$, A is Q and B is L;

where $i \neq 1$ and $j + 1 = n$, A is T and B is M; and

where $i \neq 1$ and $j + 1 \neq n$, A is T and B is L;

Q being selected from the group H-, H_2N-, P-HN-, RR'N-, H_2NCO-, RR'NCO-, RCO-;

M being selected from the group H-, -COOH, -COOR, $-CONH_2$, -CONRR' and -NHCOR;

L being $-CO-NH-CH(R_{j+2})-CO-\ldots-NH-CH(R_n)-CO-Y$

wherein Y is selected from the group -OH, -OR, $-NH_2$, and -NRR'; and

T being $X-HN-CH(R_1)-CO-\ldots-NH-CH(R_{i-1})CO-NH-$

wherein X is selected from the group H-, P-, R- and RCO-;

wherein

R_1 is CH_2SH, R_2 is H, R_3 is CH_2OH, R_4 is H, R_5 is $CH(CH_3)_2$, R_6 is $(CH_2)_3NHC(NH)NH_2$, R_7 is H, R_8 is CH_2COOH, R_9 is $CH_2(C_6H_5)$ or CH_2OH, R_{10} is H, R_{11} is CH_2OH, R_{12} is $CH_2CH(CH_3)_2$, R_{13} is CH_3, R_{14} is C_3H_6 or $CH_2CH(CH_3)_2$, R_{15} is $(CH_2)_3NHC(NH)NH_2$, R_{16} is $CH(CH_3)_2$, R_{17} is CH_3, R_{18} is $(CH_2)_3NHC(NH)NH_2$, R_{19} is $CH_2CH_2C(O)NH_2$ and R_{20} is $CH_2CH(CH_3)_2$,

R and R' are independently selected from the group hydrogen, C_{1-25} alkyl, C_{3-25} allyl, C_{6-25} aryl, benzyl, 2-phenyl-ethyl, methyl-fluorenyl, glycolamide and benzhydrylglycolamide; and

P is a protecting group;

wherein the composition further contains a diluent.

5. I have been advised that the U.S. Patent Office official responsible for the above-identified application has asserted that the above-identified application fails to teach one of ordinary skill in the art of foot-and-mouth disease and veterinary vaccination, for example, how to make and use the above-described subject matter.

6. I believe that the above-identified application teaches one of ordinary skill in the art of foot-and-mouth disease and veterinary vaccination, for example, how to make and use the above-described subject matter. I believe that any additional effort required by one of ordinary skill in the art to make and use the above-described subject matter would constitute, at most, a reasonable amount of experimentation or routine experimentation.

7. I have been advised that the U.S. Patent Office official responsible for the above-identified application has asserted that one of ordinary skill in the art could not have reasonably predicted the effects of chemical modifications at single or multiple amino acid locations throughout the peptides of the above-described subject matter on the immunological and biochemical properties of any given peptide.

8. I believe that the above-described subject matter does not involve chemical modifications at single or multiple amino acid locations throughout the peptides. I understand that the peptides are modified in the above-described subject matter to include modifications in the peptide backbone, as compared with the recited native peptides, in substituting -NH-CO- groups for -CO-NH groups. Moreover, modifications are possible in the ends of the peptides.

9. I believe that one of ordinary skill in the art reviewing the above-identified application and art available at the time the application was filed, would have reasonably expected that the above-described subject matter could be made and used with, at most, a reasonable amount of experimentation or routine experimentation. Further, I believe that one of ordinary skill in the art would not have required an absolute predictability in the teaching of the above-identified application as to how the described modifications to the native peptide may have effected the immunological and/or biochemical properties of any given peptide, as one of ordinary skill in the present art would be able to screen the above-described compositions, with a reasonable amount

of experimentation, to determine the immunological and/or biochemical properties of the compositions. I believe the above-identified application and art available at the time of the invention, for example, describe how to make the above-described compositions and screen for the required immunological and/or biological properties.

10. I believe that one of ordinary skill in the art will be able to construct the above-described compositions with, at most, a routine amount of experimentation, and screen the compositions for the required activity.

11. I believe that the above-identified application provides more than adequate guidance for one of ordinary skill in the art to make and use the above-described compositions. Specifically, for example, the above-identified application provides, as Example 3, an illustration of vaccination of a totally retro-partly inverso peptides corresponding to the major antigenic determinant situated on the protein VP_1 of the virus of aphthous fever (foot-and-mouth disease virus, FMDV).

One of ordinary skill in the art will have appreciated that protein VP_1 was known to trigger synthesis of neutralizing antibodies (Ab).

Moreover, one of ordinary skill in the art will have appreciated that vaccines existed conventionally in two forms, attenuated or inactivated, but their preparation and their handling presented many disadvantages. At the time the present invention, several groups of researchers in the field of FMDV had studied the possibility of producing significant quantities of the protein VP_1 by means of genetic engineering

techniques. However, the doses needed to induce protection in cattle, as for the natural protein VP_1 isolated from viral particles, was still thought to be too high.

Another proposed approach has constituted imitation of the fragment 141-160 of the protein VP_1 by chemical synthesis. This fragment corresponds to a particular region of the protein VP_1, to which the neutralizing antibodies attach specifically. This same peptide coupled to a carrier protein induces an immune response in the guinea-pig such that the immunized animal is protected against aphthous fever. These animals are a very good biological model for study of the disease. It has been found that a single injection of conjugated peptide was sufficient to protect infected animals.

However, fundamental research was still thought to be necessary to provide these synthetic peptides with their entire effectiveness as vaccines and it has often proved to be difficult to obtain sufficient neutralizing titres of anti-peptide Ab. This was thought to be related to the problems relating to stabilization of an "optimum" conformation of a linear sequence, as well as to the rapid degradation of peptides injected into the animal.

12. The above-identified application describes studies of the antigenic and immunogenic properties of retro-inverso (RI) analogues derived from the immunodominant loop of three variants of serotype A12 of FMDV. The sequences of these peptides and of the corresponding RI analogues are shown in Table 8 of the above-identified application. The above-identified application describes as how a cysteine residue was added in the N-terminal position at the end of coupling.

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The study of the above-identified application was divided into the following three parts: (1) study of the antigenic properties of the analogues; (2) study of the immunogenic properties of the analogues and (3) study of the immunogenic properties of the analogues: neutralizing response.

In the first part of the study, the antigenic properties of the analogues were investigated. The results are shown on Table 9 of the above-identified application. The two RIa and RIb diastereomers were separated, purified by HPLC and tested separately in ELISA. The RI isomer eluted fastest by HPLC is called RIa, and the 2nd peak eluted (isomer eluted slowest) comprises the isomer called RIb. Only the results with the FP system are shown. One of ordinary skill will appreciate that the RI analogues were recognized as well as and often better than the parent FP-L peptide. The results are reported to be analogous in the case of the FL and SL peptides.

Table 10 of the above-identified application shows the amounts of analogues which are necessary to inhibit by 50% the bonding of the various antibodies to the parent FP-L peptide immobilized on a dextran matrix (by cysteine). The effect of the position of the cysteine in N- or C-terminal and the effect of blocking the C-terminal end or the two N- and C-terminal ends were studied and the blocked or non-blocked RI analogues were all noted to be competitors which were as good as the parent FP-L peptide.

In the study of the immunogenic properties of the analogues, the parent (L) peptide and the RIa and RIb analogues were injected into rabbits and the ELISA response with respect to the homologous peptides was measured. The results are shown with the FL peptide in Table 11 of the above-identified application. The FL-RIb

peptide was shown to have induced antibody titres 8 times higher in the "Cannes" rabbit. The recognition of the various analogues by the rabbit anti-peptide antibodies were tested by the same principle as that shown in Table 10 of the above-identified application, using the analogues in solution in the BIAcore system (Table 12, competition test of the above-identified application).

In the study of the immunogenic neutralizing response of the analogues, the L and RIb FP peptides were injected into guinea-pigs and the neutralizing response on the virus was measured *in vitro*. The preparations used correspond to peptide analogues bonded to liposomes of the small unilamellar liposome type. The neutralization test was carried out by methods known in the art. The results are shown in Table 13 of the above-identified application. The results are expressed as $\log_{10}$ and correspond to the difference between the titre of the virus incubated with normal serum and that of the virus incubated with serum of the immunized guinea-pig (dilution of the sera 1/20).

It is noted that the effectiveness of the FP-L peptide is similar to that of the same peptide described previously and that these results are reproduced entirely with the RI FP peptide.

As further detailed in the above-identified application, the *in vitro* neutralization titers of the sera taken at various intervals were followed for 362 days. The results showed that the level of the response to the retro-inverso peptide NH_2-(C)141-159-OH was similar to that obtained with the L-peptides H-141-159(C)-NH_2 and H-(C)141-159-OH up to around 50 days after the inoculation. However, compared with the response to the L-peptides, the response against retro-inverso NH_2-(C)141-159-OH peptide

continued to increase beyond 50 days (the neutralizing indices are at least 10-fold higher at 100 days). In the samples collected 262 days after inoculation of the animals, the neutralizing indices of the sera from guinea pigs that received the retro-inverso peptide were reported to still be significantly higher than those of the sera from responder animals inoculated with the L-peptides.

13. The above-identified application further describes protection of swine from foot-and-mouth disease with one dose of the all-D retro peptide corresponding to the immunodominant GH loop encompassing residues 141-159 of capsid protein VP1 of foot-and-mouth disease virus serotype A, sub-type12 (FP peptide).

One of the nine vaccinated animals was completely unprotected and two developed very small lesions. None of the six remaining animals exhibited any clinical signs but two developed antibodies against non-structural proteins indicating that replication of the virus had occurred. No evidence of replication could be detected in the remaining four animals, either by rise in neutralizing antibody titre or by production of antibodies against non-structural proteins specific for virus replication.

14. Further evidence of the use of the above-described compositions is presented in the attached Nargi et al., Vaccine 17 (1999) 288-2893.

Specifically, the attached describes work relating to the vaccination of swine with an all-D retro peptide corresponding to the immunodominant GH loop encompassing residues 141-159 of capsid protein VP1 of foot-and-mouth diseases virus serotype A, sub-type 12 (FP variant). This article shows that a single inoculation of the all-D retro

peptide corresponding to the GH loop of FMDV was able to induce anti-peptide and virus neutralizing antibodies in pigs.

This article relates to the use of a totally retro-inverso peptide of FP peptide from serotype A12 of foot-and-mouth disease virus. The above-described Example 3 of the above-identified application relates to the use of a totally retro-partly inverso peptide of FP peptide from serotype A12 of foot-and-mouth disease virus. Thus, the article and the example are submitted to provide sufficient evidence for one of ordinary skill in the art that immunoretroid peptides of FP will retain the requisite immunogenicity and specificity of the parent peptide FP.

15. I believe that the above-identified application exemplifies immunoretroids of the above-described compositions and that one of ordinary skill in the art would be able to, at a minimum, make and screen the immunoretroids of the above-described compositions, with a reasonable amount of experimentation, to identify species having the required specificity.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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Signed this 24th day of FEBRUARY, 2005.

(Signature) _____
Lawrence K. Silbart

CURRICULUM VITAE: Lawrence K. Silbart, Ph.D.

Personal Data:

Name:	Lawrence K. Silbart
Born:	January 22, 1958
Marital Status:	Married, three children

Education:

High School:	Highland Park High School, Highland Park, Illinois, 1972-1976.
Undergraduate:	University of Michigan, Ann Arbor, B.G.S. (Biochemistry conc.), 1976-80
Graduate:	University of Michigan (Ann Arbor), Toxicology/Industrial Health (double concentration), 1980-83, M.P.H.
	University of Michigan (Ann Arbor), Toxicology, 1983-87, Ph.D.

Professional Training:

1981-84	Clinical Laboratory Tech., Department of Pathology, The University of Michigan Hospital.
1983-84	Staff Scientist, National Wildlife Federation-Great Lakes Natural Resource Center, Ann Arbor,
1985-87	Research Assistant, Department of Pathology, University of Michigan Medical School.
1986-87	Research Assistant, Department of Pharmacology, University of Michigan Medical School.
1988-89	Postdoctoral Research Fellow, Department of Pathology, University of Michigan.
1989-91	Research Investigator, Department of Pathology, University of Michigan.
1991-97	Assistant Professor of Animal Science, University of Connecticut, Storrs, CT.
1991-97	Joint Appointment - Assistant Professor of Molecular and Cell Biology, UCONN, Storrs, CT
1991-Present	Assistant Director, Center for Environmental Health, University of Connecticut, Storrs, CT.
1997-Present	Associate Professor of Animal Science, The University of Connecticut, Storrs, CT
1997-Present	Joint Appointment - Associate Professor of Molecular and Cell Biology, UCONN, Storrs, CT
1998-Present	Joint Appointment – Associate Professor of Pathobiology, UCONN, Storrs, CT
1997-Present	Visiting Scholar, Harvard University School of Public Health, Boston, MA
1997-Present	P.I., Center for Excellence in Vaccine Research
1998-Present	Co-Facility Head, Live Cell Sensing Unit, The University of Connecticut, Storrs, CT
1999-1999	Visiting Associate Professor, Children's Hospital, Harvard University, Boston, MA
2001-Present	Associate Director, Center of Excellence for Vaccine Research, UCONN
2002-Present	Adjunct Associate Professor of Veterinary Medicine, Tufts University School of Veterinary Medicine

Honors and Awards:

Alpha Zeta
Gamma Sigma Delta
Phi Kappa Phi (Inducted 1997)
Evans Scholarship, University of Michigan, 1976-1980
Dean's List, University of Michigan-Ann Arbor
National Honor Society, Highland Park High School
Donald M. Kinsman Award for Excellence in Undergraduate Teaching. Awarded 4/4/02
Nominated - Outstanding Advisor Award, 2003
CANR Alumni Association Teaching Award, 11/03
CANR Special Achievement Award (Merit) 1997, 2004

Teaching Activities:

Undergraduate Biochemistry by Keller Plan; One-On-One Instruction and Testing (Biology 411), 1978.
Undergraduate Physics by Keller Plan; One-On-One Instruction and Testing (Physics 241), 1979.
Eastern Michigan University-Biochemistry Laboratory. Four hour laboratory course, Winter, 1988.
The University of Michigan – Pathology 650 – Lab Techniques in Experimental Pathology, Spring '91.

Eastern Michigan University, Environmental Chemistry, Fall semester, 1990.
UCONN, ANSC 226/366 "Environmental Health." (100%) 3 credits (1991-present).
UCONN, ANSC 221 "Environment, Genetics and Cancer." (100%) 3 credits (1993-present).
UCONN, ANSC 224 "Food Safety." (50%/ with Faustman) 3 credits (1993-1999).
UCONN, ANSC 306 "Vaccinology" (50%/ with Geary) 3 credits, Spring, 2001 and 2003.
UCONN, ANSC 390 "Graduate Presentation Skill" (50% with Zinn) Spring 2001

Guest Lectures at UCONN

Path 297: Pathobiology - 3 lecture series – (past 5 years)
Cell Mediated Immunity
Humoral Immunity
Cancer Etiology
ANSC 224: Food Safety and Microbiology (Past four years)
Bovine Spongiform Encephalopathies and Mad Cow Disease,
Food Allergy
ANSC 298 (Special Topics "Mad Cow Disease" - 2 lectures) – Last year only
Pathogenesis of Prion Disease
Sporadic and Hereditary forms of human TSEs (vCJD, classical CJD)
EEB 205: Current Issues in Environmental Science (Honors) - (Past four years)
Environmental Impact of GM crops
SAAS 004: Structure and Function of the Immune System (2 lecture series – six years)
Organization of ImmuneSsystem and Innate Immunity
Adaptive Immunity (Cell mediated and Humoral)
PVS 349 (Immunobiology) (Past six years, alternate years)
Mucosal Immunology
PLSC 246 "*Allergenicity of Genetically Modified Foods*" Past three Years
CHEM 299/300 Hazardous Waste Operations and Emergency Response
"*Basic Toxicological Principles*" (twice)
ANSC 299 - Biotechnology Instrumentation (3-lecture series; given twice)
Enzyme Immunoassays
In vitro mammalian cell transfection
Fluorescence microscopy
Allied Health 211: "*Mycotoxins and Cancer*" (twice)

Invited Oral Presentations – International Meetings

Sixth International Congress of Mucosal Immunology, Tokyo, Japan. "Strategies for eliciting a mucosal immune response to the chemical carcinogens 2-acetylaminofluorene and aflatoxin B1. 7/24/90.

Nanjing Sino-America Agricultural Biotechnology Symposium. 10/10-10/12/00 - "Policy Issues Regarding the Development and Use of Genetically Modified Foods in the United States." Nanjing, China.

14th International IOM Congress. Vienna Austria. "A Modified Live Attenuated *Mycoplasma gallisepticum* Vaccine Protects Chickens from Respiratory Disease." 7/7 – 7/11/02.

Institute de Biologie Moleulaire et Cellulaire (IBMC), "Modifications within the 3'-UTR region of DNA vaccines influences antibody titers, seroconversion rates and cytokine profiles." Strassbourg, FR, 7/12/02

Invited Presentation – 15th Congress of the International Organization for Mycoplasmology, Athens, Georgia. 7/2004. Keynote Symposium II: Host Pathogen Interactions. "Correlates of Immune Protection in GT5 Vaccinated Chickens Challenged with Pathogenic *Mycoplasma gallisepticum* R_{low}."

Poster Presentations at International Meetings:

IVVAC International Meeting: . "Development of attenuated Mycoplasma gallisepticum as a modified live vaccine and vector for heterologous antigens in poultry." Oxford, U.K July 23-28, 2000. (Presented by M. Kumal)

27th U.S.-Japan Joint Conference on Cholera and Related Diarrheal Diseases. "Enterotoxins as Adjuvants and Carrier Proteins for the Elicitation of a Mucosal Immune Response to Chemical Carcinogens." Charlottesville, VA 9/91

Invited Oral Presentations (selected pre-1996): National and Regional

Invited Speaker "Development of a Radioimmunoassay for the Detection of 2-Acetylaminofluorene" U.S. EPA, April 1986, Research Triangle Park, N.C.

Detection of Cumulative Trauma Disorders Based on Urinary Excretion of a Hydroxylproline Metabolite. University of Michigan School of Public Health, Environmental and and Industrial Health Seminar, 1984.

Michigan-School of Public Health, Toxicology Seminar, "The Mucosal Immune Response to Chemical Carcinogens." 9/22/89. The University of Michigan-Immunology Colloquium, "Development of Vaccines to Block Mucosal Absorption of Chemical Carcinogens." 1/24/90.

Eastern Michigan University, "Immune System Toxicology," 2/19/90.

The American Cancer Society, Michigan Division, Cancer Research Conference, Ypsilanti, Michigan. "Development of Vaccines Capable of Eliciting a Mucosal Immune Response to Chemical Carcinogens. 6/22/90.

The American Association of Immunologists (AAI). Development of non-toxic (anti-idiotypic) mucosal vaccines to block the absorption of the chemical carcinogen 2-acetylaminofluorene (AAF). Atlanta Georgia, 4/25/91.

Note: Other pre-tenure (1996) speaking engagements are not listed.

Southern Connecticut State University, "Prospects for an AIDS Vaccine" ISIS Program, 5/97

5th Annual New England-New York Poultry Pest Management Workshop "Pesticide Toxicity" 5/97, Sturbridge, MA

Harvard University Visiting Scholars Retreat "Developing Web-based learning platforms for teaching environmental health" 7/98 Stowe, VT

University of Connecticut Health Center, Department of Pathology, "Mucosal Peptide and DNA Vaccines for HIV" 9/3/98, Farmington, CT

Harvard University, Department of G.I. Cell Biology. "Mucosal Approaches to Genetic Vaccination." Harvard Medical School. 11/5/98

Harvard University Visiting Scholars Retreat "Integrating Critical Thinking Concepts into an Environmental Health Curriculum" 7/99 New London, CT

UCONN Animal Science Seminar: "Peptide Vaccines for Mucosal Protection against HIV" 12/3/99..

Harvard University Visiting Scholars Retreat "Integrating Critical Thinking Concepts into an Environmental Health Curriculum" Portsmouth, NH, 7/00

University of Connecticut, School of Pharmacy "Mucosal Peptide and DNA Vaccines for HIV" 9/21/98, Storrs, CT

Southern Connecticut State University, "Stimulating Mucosal Immunity: The Challenge of Oral Vaccination" ISIS Program, 10/7/99

UCONN Animal Science Seminar, "Peptide and DNA Vaccines for Mucosal Protection against HIV-1" Storrs, CT 12/3/99

8th Annual New England-New York Poultry Pest Management Workshop "Pesticide Safety and Toxicologyy" 5/25/00, Sturbridge, MA

USDA/University of Missouri/UCONN Joint Vaccine Consortium Annual Meeting. "Peptide Vaccines for FMDV" Columbia, MO 8/00

Harvard University Visiting Scholars Retreat "Integrating Critical Thinking Concepts into an Environmental Health Curriculum"

New England Regional Nutrition Conference, "Genetically Modified Foods: Pro's, Con's and Controversies." Waterville Valley, NH 4/25-4/27/01.

CT Association of Dairy and Food Sanitarians - Genetically Modified Foods - Separating Scientific facts from Hysteria. New Haven, CT 5/23/01

Food Safety Policy Forum: Facilitator on Emerging Technologies section. Wesleyan University, Middletown CT, 6/14/01.

Harvard University Visiting Scholars Retreat "Integrating Critical Thinking Concepts into an Environmental Health Curriculum" 7/01 Plymouth, MA

Metanoia, UCONN – "Agricultural Biowarfare and Bioterrorism" – 11/13/2001

"The Warp and Woof of Complex Issues: Using Logic and Cognitive Science to Address Complex Environmental Issues. UCONN Dodd Research Center, March 16, 2001.

USDA/University of Missouri/UCONN Joint Vaccine Consortium Annual Meeting. "Peptide Vaccines for FMDV" UCONN, Storrs (Nathan Hale Inn) 8/01

Intranasal immunization of guinea pigs with FMDV A12 VP1 peptide-KLH conjugates induces serum neutralizing antibodies and protection upon challenge. Molecular Approaches to Vaccine Design. Cold Spring Harbor Conference, Nov 29-Dec 2, 2001.

Harvard University Visiting Scholars Retreat "Integrating Critical Thinking Concepts into an Environmental Health Curriculum" Vinal Haven Island, Maine, 7/31/02

Intranasal immunization of guinea pigs with FMDV A12 VP1 peptide-KLH conjugates induces serum neutralizing antibodies and protection upon challenge. Tufts Veterinary College. 2/7/02

Modulating gene expression using DNA vaccine with different 3'-UTRs influences antibody titer, seroconversion rate and cytokine profiles. Tufts Veterinary College. 4/18/02

Spherics Corporation: "Intranasal immunization of guinea pigs with FMDV A12 VP1 peptide-KLH conjugates induces serum neutralizing antibodies and protection upon challenge." Warwick, RI 02/21/02
UCONN CANR Graduate Research Forum, "Modulating gene expression using DNA vaccine with different 3'-UTRs influences antibody titer, seroconversion rate and cytokine profiles" 4/12/02.

World Affairs Forum, "Genetically Modified Foods - Separating fact from hysteria" Stamford, CT 3/6/02.

UCONN CANR Graduate Research Forum, 4/12/2002 Modulating gene expression using DNA vaccines using different 3'-UTRs influences antibody titer, seroconversion rate and cytokine profiles."

USDA/University of Missouri/UCONN Joint Vaccine Consortium Annual Meeting. "Peptide Vaccines for FMDV" Columbia, MO 8/02

Harvard School of Public Health Visiting Scholars Retreat. "Strategies for prevent smokeless tobacco-related cancers of the oral cavity" Narragansett, R.I. 7/26-28/03

Harvard School of Public Health – Invited participant. "Privacy, Informed Consent and Genomic Research." March 24th, 2003

USDA/University of Missouri/UCONN Joint Vaccine Consortium Annual Meeting. "Peptide Vaccines for FMDV" UCONN, Storrs (Nathan Hale Inn) 8/01

Tufts Veterinary College. "DNA Vaccines: From Concept to Clinic." Guest lecture to 2nd year Veterinary Students enrolled in the Biotechnology course. 4/18/03
Invited Participant: "Privacy, Informed Consent and Genomic Research" Harvard NIEHS Center for Environmental Health, 3/24/03

International Organization of Mycoplasmology, 15th Annual Congress, Correlates of Immune Protection in GT5 Vaccinated Chickens Challenged with Pathogenic *Mycoplasma gallisepticum* R_{low}. Athens, GA 7/14/04

Harvard School of Public Health Visiting Scholars Retreat. "Problem based Learning Exercises for Environmental Health Students" Stowe, VT 7/25/04

Harvard University - Second Annual New England Regional Symposium On Frontiers in Mucosal Immunology Mucosal Vaccines. "Developing mucosal vaccines for veterinary applications: Correlates of immune protection in chickens using a live attenujated Mycoplasma gallisepticum vaccine." September 20th, 2004 Boston, MA

Invited Speaker: UCONN Pathobiology Departmental Seminar "Mycoplasma gallisepticum vaccines: Correlates of Immune Protection" 2/26/04

Invited Speaker: University of Nebraska School of Veterinary Medicine, ""Mycoplasma gallisepticum vaccines: Correlates of Immune Protection" Lincoln, NE 2/10/04

University of Nebraska School of Veterinary Medicine, "Mucosal Vaccines" as part of their teleconference course. Lincoln, NE 2/9/04

Invited Participant: 2003 ARS Immunology Workshop, Washington D.C., 12/1 – 12/4/03

UCONN ATL Seminar Series; "A tale of three projects – Mucosal Vaccine Development for Various Applications" 4/22/04

USDA/University of Missouri/UCONN Joint Vaccine Consortium Annual Meeting. "Peptide Vaccines for FMDV" Storrs, CT, 8/04

Books and Book Chapters:

Keren, D.F., Brown,J.E., Silbart, L.K., McDonald, R.A., and Wassef, J.S. (1989) Enterotoxins as Stimulators of Mucosal Immunity: Shiga Toxin and Cholera Toxin. In: Progress in Cholera Research

Keren, D.F. and Silbart, L.K. (1992) Strategies to achieve mucosal immunity. In: Recombinant DNA Vaccines: Rationale and Strategy. pp 147-168. Richard E. Isaacson, (Ed.) Marcel Dekker,

Silbart, L.K. and D.F. Keren (1998) Structure and Function of the Gastrointestinal Immune System. In: Pathology of the Gastrointestinal Tract, 2nd edition, pp 99-113, Eds: Ming S.and H. Goldman.

Silbart, L.K., (2002) Environmental Health (246-page companion study guide for ANSC 226). Erudition Books, Courier Custom Publishing, Inc., N. Chelmsford, MA. ISBN 1-58692-439-7.

Peer-Reviewed Articles:

Keren, D.F., Silbart, L.K., Lincoln, P.M. and Annesley, T.M (1986): Significance of immune responses to mucosal carcinogens: A hypothesis and a workable model system. *Pathol. Immunopathol Res.*; 5:265-277.

Silbart, L.K., Nordblom, G., Keren, D.F., Wise, D.S., Lincoln, P.M. and Townsend, L.B.: (1988) A rapid and sensitive screening method for the detection of anti-2-acetylaminofluorene immunoglobulins. *J. Immunol. Methods.*; 109:103-112.

Silbart, L.K. and D.F. Keren: (1989) Reduction of Intestinal Carcinogen Absorption by Carcinogen-Specific Secretory Immunity. *Science*; 243:1462-1464 .

Kilbane, A.J., Silbart, L.K., Manis, M., Beitins, E.Z. and Weber, W.W.: (1990) Human N-acetylation genotype determination with urinary caffeine metabolites. J. Pharmacol. Exp. Therap.; 47(4):470-7.

Silbart, L.K., D.F. Keren, R.A. McDonald, L. Goslinoski, B. Miller, J.D. Clements, and J. Smart (1991). Strategies for eliciting a mucosal immune response to the chemical carcinogens 2-acetylaminofluorene and aflatoxin B1. *Frontiers of Mucosal Immunology* 2:469-470.

Silbart L.K., D.F. Keren, R.A. McDonald, P.M. Lincoln, L. Goslinoski, and J.B. Smart (1992). Characterization of the Mucosal Immune Response to 2-Acetylaminofluorene-protein conjugates. *Regional Immunology* 4(4):245-254.

Silbart, L.K. (1993) Stimulating Mucosal Immunity: The Challenge of Oral Vaccination. *Clinical Immunology Newsletter* 13:113-119.

Oliver, A.R., Silbart, L.K., Keren D.F., Miller,B., McDonald, R.A. (1996) Mucosal tolerance to Aflatoxin B1 Following Mucosal Immunization with Aflatoxin B1-Carrier Protein Conjugates and Cholera Toxin. *Annals of the New York Academy of Science* 778:422-425.

McAleer, F.T., Silbart, L.K., VanKruiningen, H.J., Koudelka and A. Tobias (1996). A Simplified Procedure for Studies of Intestinal Immunity in Rabbits. *J. Immunological Methods* 194:49-58.

Silbart ,L.K. McAleer, F.T., Rasmussen, M.V., Goslinoski, L., Keren, D.F., VanKruninigen, H.J. and J.M. Winchell. (1996) Selective Induction of Mucosal Immune Responses to 2-acetylaminofluorene. *Anticancer Research*, 16:651-660.

Oliver, A.R., Silbart, L.K., McDonald, R.A., Miller,B. and D.F. Keren (1997). Mucosal Unresponsiveness to Aflatoxin B1 is not broken by Cholera Toxin. *Immunology and Cell Biology* 75:47-53.

Rasmussen, M.V., Oliver, A.R. (1997) Immunoprophylactic intervention in chemical toxicity and carcinogenicity. *Veterinary and Human Toxicology*. 39:37-43.

Winchell,J.M. Van Krunininger,H.K., and L.K. Silbart, L.K. (1997) Mucosal Immune Response to an HIV C4/V3 Peptide following Nasal or Intestinal Immunization of Rabbits, *AIDS Research and Human Retroviruses*. 13: 881-889.

Rasmussen, M.V., and Silbart, L.K. (1998) Peroral Administration of Specific Antibody Enhances Carcinogen Excretion. *J. Immunotherapy* 21:418-426.

Oliver, A.R., Silbart, L.K., (1998) Local and systemic tolerance to orally administered dinitrochlorobenzene are not broken by CT. *International Archives of Allergy and Immunology*. 116:318-324.

Winchell, J.W., Routray, S., Betts, P.W., Van Kruiningen, H.J., Silbart, L.K. (1998) Mucosal and Systemic Antibody Responses to an HIV-1 C4/V3 Construct Following DNA Immunization of Rabbit Peyer's Patches. *J. Infec. Dis.* 178:850-3.

Zinckgraf, J.W., Winchell, J.M., and Silbart, L.K. (1999) Fecal and vaginal immune response to a mucosally

delivered HIV gp120-derived C4/V3 peptide *J. Repro. Immunol.* 45(2):99-112

Rasmussen,M.V., Barker T.T. and Silbart, L.K. (2001) High Affinity binding site-mediated prevention of chemical absorption ccross the castrointestinal tract. Toxicology Letters 125:51-59

Lynch, M.P., Faustman, C., Silbart, L.K., Rood, D. and Furr, H.C. (2001). Detection of lipid-derived aldehydes and aldehyde:protein adducts in vitro and in beef. J. Food Sci. 66:1093-1099.

Papazisi, L., Silbart, L.K., Frasca Jr., S., Rood, D., Liao, X., Gladd, M. Javed, M.A. and S. J. Geary (2002) A Modified Live *Mycoplasma gallisepticum* Vaccine to Protect Chickens From Respiratory Disease. *Vaccine* 20:3709-19.

Wilkinson, J., Rood, D., Minor, D., Guillard, K., Darre, M. and Silbart, L.K. (2003) Immune Response to a Mucosally Administered Aflatoxin B1 Vaccine. *Poultry Science* 82:1565-1572.

Zinckgraf, J.W. and L.K. Silbart (2003) Modulating gene expression using DNA vaccines with different 3'-UTRs influences antibody titer, seroconversion and cytokine profiles. *Vaccine* 21:1640-1649.

Fischer, D, Rood, D., Barette, R., Zuwallack, A., Kramer, E., Brown, F., and L.K. Silbart. (2003) Intranasal immunization of guinea pigs with an immunodominant FMDV peptide conjugate induces mucosal and humoral antibodies and protection upon challenge. *J. Virology* 77:7486-7491.

Manuscripts in Submission or Preparation:

Canpolat, E., Pedersen-Lane, J., Lawrence, D.A., Silbart, L.K., and Lynes, M.A. "Metallothionein interactions at leukocyte plasma membranes"

Geary, S.J. and L.K. Silbart. Vaccine development and immune protection against *Mycoplasma gallisepticum* infection in chickens. Review Article. [For submission 11/04]

Barrette, R., Urbonas, J.W., Silbart, L.K., Determination of Antigen Specific Antibody Concentration by ELISA: A Slope Correction Approach [*Clinical and Diagnostic Lab Immunol*, 11/04]

Silbart, L.K. Incorporating Problem-Based Learning Exercises into an Environmental Health Curriculum. [For submission to *J. Environ. Health*, 11/04]

Correlates of Immune Protection in GT5 Vaccinated Chickens Challenged with Pathogenic *Mycoplasma gallisepticum* R_{low}. M. Javed, M. Gladd, K. Cecchini, S. Frasca Jr., D. Rood, P. Hudson, S.J. Geary, L.K. Silbart. [For submission to *Infection and Immunity*, 11/04]

Published Abstracts

Silbart, L.K., Lincoln, P.M., Annesley, T.M. and Keren, D.F.: Selective immune response to parenteral immunization with different preparations of carrier proteins conjugated to 2-acetylaminofluorene. *Fed. Proc.* 1986; 45:698.

Keren, D.F., Lincoln, P.M., Silbart, L.K. and McDonald, R.A.: Secretory IgA response in intestinal secretions to the carcinogen 2-acetylaminofluorene (2-AAF) following combined intraperitoneal and intraintestinal administration of 2-AAF-carrier protein conjugates. *Fed. Proc.* 1987; 46:746.

Kilbane, A.J., Silbart, L.K., Manis, M., Beitins E.Z., Weber, W.W. Human acetylation genotype determination by urinary caffeine metabolites. The Pharmacologist 1988

Silbart L.K., R.A. McDonald, P.M. Lincoln, L. Goslinoski, and D.F. Keren. Elicitation of a secretory immune response to the carcinogen 2-acetylaminofluorene (2-AAF) is enhanced by conjugation to the mucosal immunogen cholera toxin. *The FASEB Journal* 1989; 3(4):A1205

Silbart, L.K., Miller, B.F., McDonald, R.A., and Keren, D.F. Secretory IgA response in rabbit intestinal

secretions to the carcinogen aflatoxin B1 (AFB1). *The FASEB Journal* 4(3) 1358A, 1990.

Keren, D.F., Silbart, L.K., Goslinoski, L., McDonald, R.A. and Smart, J. The adjuvant effect of cholera toxin, cholera toxin B subunit, and glutaraldehyde modified cholera toxin on the mucosal immune response of rabbits to 2-acetylaminofluorene-thyroglobulin conjugates. *The FASEB Journal* 4(3):1359A 1990.

Silbart, L.K., D.F. Keren, R.A. McDonald, L. Goslinoski, B. Miller, J.D. Clements, and J. Smart. Strategies for eliciting *a* mucosal immune response to the chemical carcinogens 2-acetylaminofluorene and aflatoxin B1. Conference Proceedings. The 6th International Congress of Mucosal Immunology, Tokyo, Japan (7/22/90).

Silbart, L.K., D.F. Keren, R.A. McDonald, L. Goslinoski, B. Miller, J.D. Clements, and J. Smart (1991). Strategies for eliciting *a* mucosal immune response to the chemical carcinogens 2-acetylaminofluorene and aflatoxin B1. Frontiers of Mucosal Immunology 2:469-470 (1991).

L.K. Silbart, D.F. Keren, R.A. McDonald, L. Goslinoski, B.E. Brownlee, C. Lash, J.B. Smart (1991). Development of non-toxic (anti-idiotypic) mucosal vaccines to block the absorption of the chemical carcinogen 2-acetylaminofluorene (AAF). *The FASEB Journal* 5:A966.

Miller, B.F., C.M. Toth, L.K. Silbart, R.A. McDonald, D.F. Keren, and J.B. Smart. Radioimmunoassay (RIA) for the detection of secretory antibodies to the carcinogen aflatoxin B1(AFB-B1) in rabbit and mouse intestinal secretions (1991). *The FASEB Journal* 5:A881.

L.K. Silbart, D.F. Keren, R.A. McDonald, L. Goslinoski, B.F. Miller, C. Toth, J.D. Clements, B. Brownlee, and J.B. Smart. Enterotoxins as adjuvants and carrier proteins for the elicitation of mucosal immune responses to chemical carcinogens. 27th Joint Conference on Cholera and related diarrheal diseases, A231 (1991).

L.K. Silbart, D.F. Keren, R.A. McDonald, B. Miller, L. Goslinoski, S. Williams, C. Toth, J.M. Winchell, and J.B. Smart. Secretory Immune Response to the Chemical Carcinogens 2-Acetylaminofluorene and Aflatoxin B1 (1992). The Faseb Journal 6(5):A1640

Oliver, A.R., Silbart, L.K, Keren, D.F., Miller, B., McDonald, R.A. (1993) Mucosal Immune Response Following Immunization with Aflatoxin B1 Carrier Protein Conjugates. *J. Immunology* 150(8):34A

Winchell, J.W., Silbart, L.K, Palker, T.J., Clements, J.D., Betts, P., Haynes, B. (1993) Production of immunogens to elicit an anti-HIV mucosal immune response. Engineered Vaccines for Cancer and AIDS. 9/93

Winchell, J.W., Silbart, L.K., Palker, T.J., Clements, J.D., Betts, P., Haynes, B. (1994) Production of immunogens to elicit an anti-HIV Mucosal immune response. *The Faseb Journal* 8(5):A961

Oliver, A.R., Silbart, L.K, Keren, D.F., Miller, B., McDonald, R.A. (1994). Mucosal Immune Response Following Mucosal Unresponsiveness to Aflatoxin B1 Following Immunization with AFBl-Carrier Protein Conjugates. *The Faseb Journal* 8(4):A515.

Rasmussen, M. and L.K. Silbart Specific IgA Affects Lipophilic Carcinogen Bioavailability and Partitioning (1995) *Clinical Immunology and Immunopathology,*76 (1):S96.

Winchell, J.W., Betts, P.W. and L.K. Silbart (1996) Mucosal immune responses to an HIV-1 envelope derived synthetic peptide in rabbits. Conference on Advances in AIDS Vaccine Development. AIDSLINE Abstract #35.

Winchell, J.W. and L.K. Silbart (1996) Mucosal immune responses to an HIV-1 envelope derived synthetic peptide in rabbits. American Association of Immunologists. Joint Meeting A:1191 (#1106).

Oliver, A.R. and L.K. Silbart (1996) Mucosal Priming and Tolerance Following Peroral Administration of DNCB to Mice. XXII New England Immunology Conference Proceedings. A34.

Winchell, J.M., Routray, S., Betts, P.W., Van Kruiningen, H.J., and L.K. Silbart (1997) Gene gun Vaccination

of Rabbit Peyer's Patches with an HIV C4/V3 Construct Induces Systemic and Mucosal Immunity (1997). 1st Gordon Research Conference on Genetic Vaccines, Plymouth, N.H.

Winchell, J.M., Routray, S., Betts, P.W., Van Kruiningen, H.J., and L.K. Silbart (1997) Gene gun Vaccination of Rabbit Peyer's Patches with an HIV C4/V3 Construct Induces Systemic and Mucosal Antibody Responses. HIV-1 Infection, Mucosal Immunity and Pathogenesis. NIH symposium, Bethesda, Md.

Zinckgraf, J.W., Winchell, J.M. and L.K. Silbart (1998) Nasal Immunization Followed by Vaginal Boosting Induces both Vaginal and Systemic Immune Responses to an HIV Synthetic Peptide. Experimental Biology 1998, Abst. #590, San Francisco, CA

Zinckgraf, J.W., Winchell, J.M., and L.K. Silbart (1998). Immune Responses to an HIV Peptide/DNA Construct. XXIV New England Immunology Conference, 10/15-10/16/98. Woods Hole, MA

Rasmussen,M.V. and Silbart, L.K. (2000) Modeling the abrogation of intestinal carcinogen absorption using high affinity binding sites

Wilkinson,J., Rood, Minor, D. Gillard K., Darre, M. and Silbart, L.K. (2000) Characterization of the mucosal immune response in Broiler to an aflatoxin B1-carrier mucosal vaccine. *Poultry Science* 78 (Supplement 1) p39. Poultry Science Annual Meeting, Springdale, Arkansas, August 8-11, 1999.

Zinckgraf, J.Z. and Silbart, L.K. (2000) Development of a Mucosally Delivered Inducible HIV-1 DNA Vaccine. The FASEB Journal 14 (6): A1205. American Association of Immunologist's Annual Meeting, Seattle WA, May 12th-16th, 2000.

Lynch, M.P., Phillips, A.L., Silbart, L.K., Rood, D. Waeg G. and Faustman, C. (2000) Detection of 4-hydroxynonenal oxymyoglobin adducts in vitro. 2000 Annual IFT Meeting, Dallas TX.

Kumal M., Silbart, L.K., Rood, D. Papazisi, L., Geary, S.J. (2000) Utility of High Passage R Strain of *M. gallisepticum* both as Modified Live Vaccine and as a Vector for Heterologous Antigens. American Society of Microbiology 100th annual meeting, Los Angeles, CA 5/19-5/14/00.

Kumal M., Silbart, L.K., Rood, D. Papazisi, L., Geary, S.J. (2000) *Mycoplasma gallisepticum* strain R-High as a vector for the Avian Influenza Virus Hemagglutinin (H5HA) and as a modified live vaccine. Thirteenth International Congress of the International Organization for Mycoplasmology, Fukuoka, Japan.

Kumal M., Papazisi, L, Silbart, L.K., Rood, D. Frasca, S., Geary, S.J. (2000). Development of attenuated *Mycoplasma gallisepticum* as a modified live vaccine and vector for heterologous antigens in poultry. IVVAC meeting, Oxford, U.K. July 23-28.

L. Papazisi, L. Silbart, D. Rood, S. Frasca and S.J. Geary (2001). "Development of a protective live attenuated *Mycoplasma gallisepticum* vaccine for poultry.
Conference of Research Workers in Animal Diseases, St Louis, MO.

Zinckgraf, J.W. and L.K. Silbart (2001) Development of an Inducible DNA Vaccine. Experimental Biology 2001, Abst. FASEB Journal 15(4):652 #519.3, Orlando, FL

Zinckgraf, J.W., Wohlfert, E.A., Rood, D. and L.K. Silbart (2002) Modulating gene expression using DNA vaccines with different 3'-UTRs influences antibody titer, seroconversion rate and cytokine profiles. The FASEB Journal 16: A312. New Orleans, LA 4/20 - 4/24/02.

Fischer, D, Rood, D., Barette, R., Zuwallack, A., Kramer, E., Brown, F., and L.K. Silbart. (2002). Intranasal immunization of guinea pigs with FMDV A12 VP1 peptide-KLH conjugates induces serum neutralizing antibodies and protection upon challenge. Molecular Approaches to Vaccine Design. Cold Spring Harbor Conference, Nov 29-Dec 2, 2001.

Papazisi, L., Silbart, L.K., Frasca Jr., S., Rood, D., Liao, X., Gladd, M. Javed, M.A. and S. J. Geary (2002) A Modified Live *Mycoplasma gallisepticum* Vaccine to Protect Chickens From Respiratory Disease.

Conference Proceedings: International Organization of Mycoplasmology, 14th Annual Congress, 07/10/02, Vienna, Austria.

A.L. Phillips, S. Lee, L. Silbart and C. Faustman (2002). *In-vitro* oxidation of bovine oxymyoglobin as affected by 4-hydroxy-nonenal. Reciprocal Meat Conference J. Animal Science 79:378 (Abstract #1565).

Papazisi, L., Frasca Jr. S., Gladd, M., Liao, X., Rood, D., Silbart, L. and S. J. Geary, 5/02. "CrmA is Essential for *Mycoplasma gallisepticum* Cytadherence and Virulence, Conference Proceedings: American Society for Microbiology National Meeting, Salt Lake City, UT.

Canpolat, E., Pedersen-Lane, J., Lawrence, D.A., Silbart, L.K., and Lynes, M.A. 2002 "Metallothionein interactions at leukocyte plasma membranes" Conference Proceedings: Northeast Society of Toxicology, Groton, CT

Canpolat, E., Pedersen-Lane, J., Lawrence, D.A., Silbart, L.K., and Lynes, M.A. 2003 "Metallothionein interactions at leukocyte plasma membranes" Conference Proceedings:Society of Toxicology Annual meeting, Salt Lake City, UT

Canpolat-Turgut, E., Silbart, L.K., Lynes, M.A. "The effect of an anti-metallothionein monoclonal antibody (UC1MT) on anti-FMDV response" Conference Proceedings: Northeast Society of Toxicology Cambridge, MA 11/14/03

Correlates of Immune Protection in GT5 Vaccinated Chickens Challenged with Pathogenic *Mycoplasma gallisepticum* R_{low}. M. Javed, M. Gladd, K. Cecchini, S. Frasca Jr., D. Rood, P. Hudson, S.J. Geary, L.K. Silbart. University of Connecticut, Center of Excellence for Vaccine Research, Storrs, CT Abstract and oral presentation (M. Javed), CRWAD meeting, November 12-14, 2004, Chicago IL.

Non-peer reviewed articles:

Silbart, L.K. (1997) Mucosal Immunity and Protection from Chemical Carcinogens. Center for Environmental Health Newsletter, May 1997.

Academic Advising:

High School Students (laboratory training/exercises)

Laura Kubica, Glastonbury High School
Glen Billings, Glastonbury High School
Beth Grossman, Glastonbury High School
Jasper Connor, NIH NCRR High School Student Apprentice Program
Larissa Consing, NIH NCRR High School Student Apprentice Program
Brian Burgess, Morgan High School, Clinton, CT
Philip Licitra, Glastonbury High School
Lauren Dugdale, Glastonbury High School
Laura Mothersele, Glastonbury High School
Rebecca Sawyer, Glastonbury High School

Undergraduate Academic Advisees [Environmental Health or Individualized Majors]

Mary LeMieux (individualized major)
Irene Checchin
Poly Ingraham
Rob Hartley
Elizabeth Peterson (University Scholar)
Brook Reynolds
Tom Barrett

Jamie D'Agostino
Cara Endyke
Robin Fiorente
Rachel Grabowski
Larissa Graham
Alicia Heffernan
Julianna Kristoff
Julie Hansen
Laura Thibodeau
David Thomas
Madalina Totolici
Joe Zavalishin
Tonia Vassilowitch
Sheila Kitchen
Sheryl Kitchen
Nina Carte
Ashley Kay
Diana Orlando
Alaina Risotti
Louis Tuohy
Christy Quagliaroli
Amanda Duran, Pre-Vet
Curt Ciarleglio, Pre-Vet
Zacharie Goodreau, Pre-Vet

Undergraduate Independent Study Students Performing Laboratory Investigations/Honors Thesis
*(an * denotes undergraduate students who were co-authors on peer-reviewed scientific papers)*

Soumya Routray*
James Samuel (Honors Thesis)
Cara Endyke
Frank McAleer*
Jan Koudelka*
Allison Tobias*
Adriene Zuwallack*
Devon Minor*
Beth Wolfert*
Jessica Urbonas * (publication pending)
Daniel Zapata
Gretchen S Scheibel
Konstantina Gialelis
Kristen Digiulio
Lindsey Segundo

Master's Degree Advising:

John Wilkinson, M.S., Animal Science - Primary Advisor (Defended 2000)
Richard Johnson, M.S., Chemistry, Associate Advisor (Completed, 2002)
Courtney Snyder, M.S., (Plan B) Animal Science, Primary Advisor (Completed, 2001)
Daniela Fischer, M.S., Molecular and Cell Biology, Primary Advisor (Completed, 2002)
Omar Delgado, M.S.., (Plan B) Molecular and Cell Biology, Primary Advisor (Completed, 2002)
Letisha Wubbel, M.S. (Plan B), Animal Science (Completed 2001)
Casey Moyes, M.S., Animal Science, Associate Advisor (Completed, 2004)
Tolga Barker, M.S., Primary Advisor, Animal Science (Completed, 2003)
Eric Ling, M.S., Associate Advisor, Pathobiology
Chandrika Rajan, M.S., Associate Advisor, Pharmacy
Evan Barry, M.S., Animal Science, Primary Advisor (Plan B)
Sheila Tucker, M.S., Animal Science, Primary Advisor (Plan B)

Nikoletta Kallinteris, M.S.,, Molecular and Cell Biology, Associate Advisor (Completed, 2001)
Ahmet Okur, M.S., Associate Advisor, Pathobiology, (Completed 2001)
Derek Stevens, MCB, Primary Advisor (Completed 2003)
Erica Poulin, PVS, Associate Advisor
Pamela Malchoff, Animal Science Plan B M.S., Primary advisor

Ph.D. Degree Advising:

Jonas Winchell, Ph.D., Molecular and Cell Biology - Primary Adviser (Completed 1997)
Alfred Oliver, Ph.D., Animal Science - Primary Advisor (Completed, 1997)
Max Rasmussen, Ph.D., Animal Science - Primary Advisor (Completed 1999)
Michele Barber, Ph.D., Pathobiology - Associate Advisor (Completed 1998)
Lisa Borghesi, Ph.D., Molecular Cell Biology - Associate Advisor (Completed, 1995)
Jeehee Youn, Ph.D., Molecular and Cell Biology - Associate Advisor (Completed, 1996)
Warren Brooks, Ph.D., Molecular and Cell Biology - Associate Advisor (Completed, 2002)
John Zinckgraf, Ph.D., Molecular and Cell Biology – Advisor (Completed, 2002)
Michelle Elliott, Ph.D., Pathobiology, Associate Advisor
Michael Lynch, Ph.D., Animal Science, Associate Advisor (Completed 1999)
Emel Canpolat, Ph.D. Molecular and Cell Biology, Associate Advisor
Leka Papazisi, Ph.D. Pathobiology, Associate Advisor (Completed, 2002)
Michael Goedken, Ph.D., Pathobiology, Associate Advisor
Milton Levin, Ph.D., Pathobiology, Associate Advisor (Completed, 2004)
Jiali Tang, Ph.D., Animal Science, Associate Advisor
Roger Barrette, Ph.D., Primary Advisor, Animal Science
Mohammed Javed, Ph.D., Primary Advisor, Animal Science
Giovanni Rompato, Ph.D. Associate Advisor, Pathobiology
Rupa Challa, Ph.D., Primary Advisor, Animal Science
Shafiuddin Shafiuddin, Ph.D., Primary Advisor, Animal Science
Meghan May, Ph.D. Pathobiology, Associate Advisor
Haibing Yang, Ph.D. Plant Science, Associate Advisor
Manoj Kumar, M. Ph.D., Animal Science, Associate Advisor
Suman Surendranath, Ph.D., Animal Science, Associate Advisor
Charudharshini Srinivasan, Ph.D., Associate Advisor, Pharmacy
Bo, Dai, Ph.D., Associate Advisor, Animal Science (CRB)

Post-Doctoral Fellows Supervised:

Andrew Finley, Ph.D.
C.K. Pai, Ph.D.
John Zinckgraf, Ph.D.

Professional Development:

High Performance Liquid Chromatography (HPLC) Training Course, March 11th – 13th, 1991, Beckman Instruments, Ann Arbor, MI

Audited a laboratory course in molecular biology techniques taught in MCB, Spring 1992.

Sabbatical Leave (Invited Visiting Associate Professor) 1/4/99 to 8/20/99, Department of Pediatrics, Harvard Medical School and G.I. Cell Biology Laboratory, Children's Hospital, Boston, MA (Sponsor: Dr. Marian Neutra).

Visiting Scholar, Harvard University School of Public Health. Attended approximately five seminars and roundtables per year, plus a three-day retreat for each of the past six years. These seminars focus on environmental and occupational health issues, epidemiology, toxicology and risk assessment. The program is coordinated by Ms. Ann Backus.

NIH Grant Writing Regional Seminar, Naragansett Bay Campus, URI 8/13/02 – all day seminar entitled "Grant Writing for Success: insights and Helpful Hints on Application Preparation" (Dr. A.M. Coelho, presenter).

Flow Cytometry Training, Becton-Dickinson, FACSCalibur Sort Key Operator (4-day training course). June 22nd to 26th, 1998, Mansfield MA.

Biacore (Surface Plasmon Resonance) Training Course (two-day) "BIA Basics." San Diego, CT 7/01

Biacore (Surface Plasmon Resonance) Training Course (one-day) "Kinetics and Affinity," Chicago, IL 11/01

Public Service/Outreach Activities:

CEH Conference - "Incorporating Molecular Mechanisms into Estimates of Cancer Risk." April 23 & 24, 1992 (UCONN Bishop Center)

CEH Conference - "Pollution Prevention: From Policy to Pavement," April 8 & 9, 1993 (UCONN Bishop Center)

CEH Conference - "Genetic Predisposition to Cancer." May 6, 1994 (UCONN Bishop Center)

CEH Conference - "Breast Cancer." April 6, 1995 (UCONN Bishop Center)

CEH Conference – "Health Risks of Farming", all day conference 12/12/96 Bishop Center, Storrs, CT

CEH Conference - "Fungal Toxins: Challenges to Agriculture and Food Safety. 12/15/98

Listeria: Issues and Strategies, September 21st and 22nd, 2000. Bishop Center, UCONN Served as co-organizer with Diane Hirsch and the Food Safety Team

Particulate Air Pollution and Human Health. UCONN Dodd Center, 12/10/00

Organized and Chaired Conference entitled: "Cooperative Decision Making in Managing Connecticut's Enduring Superfund Sites" Dodd Center, 1/26/01

Sponsored Photo exhibit by Mr. Earl Dotter - "A Quiet Sickness" 1/25 - 3/16/01. Exhibit was the subject of many newspaper articles, including a feature article in the Hartford Courant.

Organized and Hosted a Visiting Scholars (Harvard University) Mini-conference entitled "The Warp and Woof of Complex Issues: Using Logic and Cognitive Science to Address Complex Environmental Issues. UCONN Dodd Research Center, March 16, 2001.

CEH Conference: Genetically Modified Foods: Impacts on Human Health and the Environment: Served as Conference co-organizer (with Dr. Chris Simon, EEB) – 2 day conference with 13 guest speakers).

Also worked with a variety of students to develop nearly 400 web pages that provide the public with information on environmental health issues.

Field frequent telephone calls regarding Environmental Health Issues from the general public.

University Service:

Departmental:

Building Safety Committee (chair, 9 years)
Graduate Committee (chair, 6 years)
G. White Building Renovation Committee (2 years)

Search Committees:
ANSC Large Animal Cloning (Dr. Jerry Yang)
ANSC Department Head – (Dr. Ian Hart)
ANSC/CRB Molecular embryologist – (Dr. Cindy Tian)
ANSC/CRB Oocyte Developmental Biologist –(Dr. Ted Rasmussen)
ANSC (Chair) Food Microbiology search, (Dr. Kumar Vankitanarayanan)
ANSC/CEH Food allergy/toxicology; first search was unsuccessful, search has been re-opened

College:

Dean's advisory committee on PTR (2 years)
Food Safety Team (5 years)
Agricultural Biotechnology Team (rarely meets)
Faculty Advisor, Alpha-Zeta (Agricultural Honor/Service Fraternity – 2 years)
Dean's Faculty Advisory Council – 2 years
Wildlife Team – 1 year
Distance Learning Committee – 2 years

Search Committees (non-ANSC)
Center of Excellence For Vaccine Research – Associate Professor in Residence (Dr. Lynn Rust)
Center of Excellence For Vaccine Research – Assistant Professor in Residence (Dr. Tim Gorton)
Pathobiology and Veterinary Science Department Head (Search unsuccessful – twice)
Department of Nutrition, Functional Foods –Dr. Steven Davis
Flow Cytometry and Confocal Microscopy Core facility; Facility Scientist – (Dr. Michele Barber)
Flow Cytometry and Confocal Microscopy Core facility; Facility Scientist – (Currently Open)

University

Laboratory Safety Committee (Chair, 6 years)
Environmental Science Undergraduate Program Steering Committee (8 years)
Toxicology Program Steering Committee (10 years)
Graduate Faculty Council (two, 3-year terms)
Ad Hoc Investigations Committee (ERI) – Scientific Misconduct (4 months)
Institutional Biosafety Committee (2 years)
Environmental Science Steering Committee (for reformation of ERI; 1 year)
Conflict of Interest Committee (2 years; Chair 2004 - 2007)
Strategic Planning Team – Center for Public Health and Health Policy (1 year)
- Academic Program Development Task Force (1 year)

Grant Proposals and Manuscripts Reviewed as Ad Hoc or Panel Member:

Federal Grant Review Panels:

National Institutes of Health Special Emphasis Panel – RFA-03-017 "Cooperative Research for the Development of Vaccines, Adjuvants Therapeutics and Diagnostics for Biodefense (VATID) and SARS" 2/17 – 2/19/04

USDA Animal Health (Panel B) – National Research Initiative Competitive Grants Program Panellist 5/3 - 5/7/04

USDA Animal Health (Panel B) - National Research Initiative Competitive Grants Program Panellist – [Invitation accepted – panel will convene in 4/2005]

[Note: Declined two invitations to serve on NIH study panels (due to conflict of interest (1) and insufficient familiarity with subject area (1)].

Ad Hoc Federal Grants Reviewed:

Department of Veterans Affairs, Office of External Reviews

U.S. Civilian Research and Development Foundation (CRDF)

USDA Animal Health

University Grant Review Panels:

Chair of UCRF Research Advisory Council's Life Sciences Review Panel, Fall 2000 – June 2001 (two cycles – 29 proposals).

Panelist for the UCRF Research Advisory Council's Life Science Review Panel:
Written reviews prepared for 18 proposals (1996/7).

American Cancer Society – Institutional Research Grant Program (UCHC – two three-year cycles – many proposals).

Center for Environmental Health Small Grants program – 2 years

Many prospectus/dissertation proposals and general examination committees for Pharmacy, Pathobiology, MCB and Animal Science Students.

Ad Hoc Reviewer of Manuscripts for the following Journals:

J. Interferon and Cytokine Research
Vaccine
J. Immunological Methods
J. Animal Science
J. Food Science
Clinical and Diagnostic Laboratory Immunology
J. Pharmacology and Experimental Therapeutics
Avian Pathology

Grants and Fellowships Held (1991-Present)

Federal Extramural Grants Funded; 1991- Present

USPHS (NIH) National Cancer Institute: "Mucosal Immune Response to Aflatoxin B1" 9/6/91 – 4/30/94 $276,000.

USPHS (ATSDR) "Environmental Health Conferences" 9/92-9/93 $4,976.

US-PHS (NIH; NIAID, NCVDG) "Peptide Immunogens for mucosal and Systemic HIV Vaccines. P.I. Barton Haynes (Duke University). UCONN Sub-project (LKS) $351,360. 12/94 to 11/97

Bioadhesive microspheres for oral DNA Vaccination. Spherics Inc. (Subcontract on NIH SBIR grant, 9/15/00 - 9/15/01) $ 22,695 Direct Costs.

USDA Equipment Grant: Expression Studies by Real-Time PCR – Request for Equipment P.I.: Dr. Susanne Von Bodman. Silbart – one of five co-P.I.'s.
Total Direct Costs Requested: $20,000 (shared instrument)

Development of Mucosal Peptide Vaccines for FMDV. USDA-NRI $200,000 (2003-2005).

Development of Mucosal Peptide and DNA Vaccine for FMDV. USDA Special Grant, Direct cost $381,203 (1999-2004)

Mycoplasma gallisepticum Vaccine. USDA Special Grant, Direct cost: $363,909 (1999-2004)

Miscellaneous Extramural Funding:

Connecticut Innovations Inc. (CII) "Development of a Mycoplama gallisepticum strain as a live-attenuated vaccine and vector for the protection of chickens and turkeys from respiratory disease. Co-P.I of project with Drs. Geary, Markus and Sekellick). Direct costs: $78,668 (LKS); overall grant $300,000.

Smokeless Tobacco Research Council: "Continued Development of Mucosal Vaccines for Carcinogens." 7/91 to 6/93 $171,882

Protein Sciences Inc. "Vaccines trials for avian influenza virus." 6/1/97 – 5/31/98 (Co-P.I. with Michael Darre – 50%) $23,143

Harvard University Stipend - $1,000 award for computer purchase in support of developing web-based learning platforms. 7/2000.

Total Extramural Funding (1991-present): $1,871,000.

Competitive Intramural Funding (UCONN):

UCRF Faculty Large Grant: Elicitation of a Mucosal Immune Response to HIV Synthetic Peptides" 1/93 – 12/93 $10,024.

UCRF Faculty Large Grant: The Influence of anti-carcinogen antibodies on mucosal absorption of carcinogens. 1/94 to 12/94 $13,889.

UCRF Faculty Large Grant: Reduction of oral mucosal DNA damage by carcinogen-specific salivary immunity. $6,657

UCRF Faculty Large Grant Developing DNA Vaccines to Block Latex Allergy, Competition, $14,159 (funded 1/04 to 12/04)

UCRF Faculty Large Grant – Genetic Vaccination to Induce Mucosal Immunity to HIV-1. 1/1/98 – 12/31/99 $15,000

UCRF Major Equipment Grant – FACSCalibur Fluorescence Activated Cell Sorting Core Facility (Co-P.I. with Michael Lynes, MCB) $72,665

Hatch Projects:

Mucosal Immunosuppression following immunization with AFB1-Protein conjugates. 10/92 to 9/95 $41,510

Mucosal Immune exclusion of Dietary Aflatoxin B1 in Broiler Chickens via active and passive immunity. 10/95 to 9/98 $49,884.

Development of a mucosal Mycoplasma gallisepticum vaccine for poultry. 10/98 to 9/01 $26,946.

Mycoplamsa Mucosal Vaccine, 10/01 to 9/04. $33,342.

Proposals for submission/re-submission:

Development of Rapid Response Preventive Agents in the Event of Deliberate Release of FMDV to Livestock. P.I. of subproject submitted by U. of Maryland
Sponsor: Department of Homeland Security. Direct Costs: $588,394

Investigating the role of outer membrane protein A in the virulence of *Enterobacter sakazakii*. USDA-NRI. $207,704. K. Venkitanarayanan (P.I.), L.K. Silbart, and Salvatore Frasca (Co-investigators)

DNA Vaccines activate regulatory T cells, blocking latex allergy, NIH-NIAID $775,250.

News Media

College of Ag. & Nat. Res. Journal 2(2):5-6 1995 "College scientist conducts research on AIDS, breast cancer, farm odor pollution and toxins in food."

"Studying the impact of environment on health" Lead Story. Hometown. April 7, 1994.

Longevity Magazine: "The war against cancer..." January, 1993

UCONN Advance – Feb 9 1998 "Faculty Experts offer insights on danger of biological warfare in Middle East.

Radio interviews: WILI and WHUS – 97/98

UCONN Advance; November 19th, 2001 "Bioterrorism Threat Real, But Not Cause for Panic."

Professional Organizations or Societies:

The American Association for the Advancement of Science
The Society for Mucosal Immunology
The American Association of Immunologists
The American Society of Investigative Pathology
The American Chemical Society
The American Society of Microbiology
The International Association of Mycoplasmology
Society for Mucosal Immunology
New England Society of Toxicology